UNITED STATES
NUCLEAR REGULATORY COMMISSION
OFFICE OF NUCLEAR MATERIAL SAFETY AND SAFEGUARDS
WASHINGTON, D.C. 20555-0001

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NRC INFORMATION NOTICE 2002-19: MEDICAL MISADMINISTRATIONS CAUSED BY FAILURE TO PROPERLY PERFORM TESTS ON DOSE CALIBRATORS FOR BETA- AND LOW-ENERGY PHOTON-EMITTING RADIONUCLIDES

Addressees:

All nuclear pharmacies and medical licensees.

Purpose:

The U.S. Nuclear Regulatory Commission (NRC) is issuing this Information Notice (IN) to (1) inform addresses of the lessons learned from an event involving multiple misadministrations due to inaccurate measurement of dosages of beta-emitting radiopharmaceuticals and (2) remind them of the importance of conducting proper tests of the dose calibrator when measuring beta- and low-energy photon-emitting radiopharmaceuticals and liquid brachytherapy sources (e.g., samarium-153, strontium-89, yttrium-90, phosphorus-32, and iodine-125). It is expected that recipients will review the information for applicability to their facilities and consider actions, as appropriate, to avoid incorrect calibrations and similar problems. However, suggestions contained in this IN are not new NRC requirements; therefore, no specific action or written response is required.

Description of Circumstances:

In December 2001, NRC became aware of 61 medical misadministrations at nine Midwestern hospitals that occurred between 1997 and 2001 as a result of inaccurate measurement of the samarium-153 unit dosages by a commercial nuclear pharmacy. The hospitals were not required to measure the dosages in dose calibrators because they ordered unit dosages of the beta-emitting radiopharmaceutical from a nuclear pharmacy licensed under 10 CFR Part 32 [see 10 CFR 35.53(b)]. In these cases, as provided in NRC's regulations, the hospitals relied solely on the nuclear pharmacy to provide the correct dosages of beta-emitting (samarium-153) radiopharmaceuticals. In 1994, another medical licensee reported potential phosphorus-32 and strontium-89 misadministrations caused by the licensee's use of a dose calibrator that was not properly calibrated for those radionuclides or the geometry of the material being measured.

Discussion:

Potential Sources of Errors in Measurement of Beta- and Low-Energy Gamma-emitters

The response of well-type gas-ionization chambers (e.g., dose calibrators) to pure beta-emitting radionuclides as a function of source geometry is complex. The spacial shape of the source can result in differences of self-absorption, and different-density containers can result

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in different attenuations that affect the accuracy of the dose calibrator readings. When the primary radiation measured is bremstrahlung, the effect may be the opposite of that expected. For example, increases in atomic number “Z” of the material containing the liquid beta-emitting radionuclide can in some instances increase the response of the ionization chamber because of the effect of the increased Z number on bremstrahlung production. This is caused both by the increase in average energy, and the intensity of the bremstrahlung radiation produced in higher Z materials.

When measuring liquids containing high-energy photon-emitting radionuclides, the effects of source shape or increase of volume is minimal. However, both low-energy photon-emitters and beta particles show increasing dependence on source volume changes as a function of decreasing energies.

Inaccurate Measurement of Samarium-153

On December 14, 2001, an NRC-licensed nuclear pharmacy reported that it had discovered that during the period July 23, 1997, to December 14, 2001, unit dosages of samarium-153 were distributed to nine of its client hospitals with approximately 28 percent less activity than the amount prescribed by the physician. The error was discovered on December 12, 2001, while filling an order of samarium-153. One of the licensee’s pharmacists questioned why a 3-cubic centimeter (cc) plastic syringe known to contain 88 millicuries read 120 millicuries in the dose calibrator. Subsequently, the licensee determined that it had failed to determine appropriate geometry and attenuation correction factors for its dose calibrator for the measurement of dosages of samarium-153.

NRC determined that the root cause of the misadministrations was the nuclear pharmacy’s failure to correct the dose calibrator response to accou

nt for attenuation of beta radiation in the plastic syringes used to dispense the radiopharmaceuticals. The licensee was unaware that a correction factor was needed to account for attenuation of the beta radiation and geometrical differences of plastic syringes. The licensee was using a correction factor, provided by the original manufacturer and distributer of the samarium-153, that applied only to a 10 cc glass vial and did not account for the effect of using less dense materials, such as plastic syringes. The manufacturer stated that its correction factor should be used for all future assays of samarium-153 in 10 cc glass vials only. The nuclear pharmacy did not realize that the correction factor would change if the dosage was measured in a plastic syringe rather than in the 10 cc glass vial.

The calibration error subsequently contributed to the incorrect activity reported on the radiopharmaceutical labels and the 61 misadministrations at the nuclear pharmacy’s nine client hospitals.

Inaccurate Measurement of Phosphorus-32 and Strontium-89

In 1994, an NRC licensee reported 14 potential misadministrations for a strontium-89 radiopharmaceutical. In that case, the licensee routinely ordered glass vials containing 4.0 millicuries of strontium-89 from the nuclear pharmacy and remeasured the activity of strontium-89 pulled up into a plastic syringe. The activity measured in the syringe was always higher than the activity the authorized user requested on the written directive. The licensee, believing its dose calibrator measurements to be more accurate than the value provided by the commercial nuclear pharmacy, adjusted the dose until the dose calibrator registered a value the licensee believed to be 4.0 millicuries. The mistake was not identified until the pharmacy delivered one of the dosages in a plastic syringe instead of the requested glass vial. When the licensee's dose calibrator indicated the activity in the syringe was over 20 percent higher than the activity requested from the pharmacy, the pharmacy was contacted.

On further investigation by the licensee into the proper dose calibrator procedures for measuring both phosphorus-32 and strontium-89, it was discovered that in addition to the failure to calibrate the dose calibrator for the differences in geometry between the vials and syringes and the differences in materials between glass and plastic, the wrong dose calibrator settings had been used.

Although there were no misadministrations, because some of the licensee's errors counteracted other errors, this case points to the difficulties licensees can have if they do not properly calibrate their dose calibrators for pure beta emitters.

Accurate Measurement of Beta- and Low-Energy Photon-Emitting Radionuclides

The importance of accurately measuring the activity of pure beta- and low-energy photon-emitters is a potential problem for all commercial nuclear pharmacy and hospital-based measurements, because of the introduction of new therapeutic products containing pure beta emitters, and the increased use of these products and low-energy photon emitters by larger numbers of licensees. In addition to the existing phosphorus-32 and strontium-89 radiopharmaceuticals, licensees are beginning to use new products such as liquid iodine-125 brachytherapy sources, yttrium-90 microsphere brachytherapy sources, yttrium-90 labeled monoclonal antibodies, phosphorus-32 coated balloons, and gas brachytherapy sources.

Commercial nuclear pharmacy licensees preparing radiopharmaceuticals containing beta- and low-energy photon-emitting radionuclides are reminded of the importance of conducting appropriate dose calibration tests for accuracy, linearity, and geometrical variation, as required in 10 CFR, 32.72(c) and (c)(1). (Medical use licensees required to measure the activity of beta-emitting radionuclides must follow similar requirements in 10 CFR 35.52, "Possession, use, calibration, and check of instruments to measure dosages of alpha- or beta-emitting radionuclides.") When performing these required dose calibration tests, licensees should consider attenuation characteristics of the beta- and low-energy photon-emitters. The radiopharmaceutical, liquid brachytherapy source, and gas brachytherapy source manufacturers can be an important source of information for the appropriate test needed to correctly calibrate your dose calibrator to accurately measure their products.

A number of manufacturers, recognizing the difficulties involved with accurately measuring the activities of pure beta- and low-energy photon-emitters, have gone to considerable effort to provide specific dose calibrator calibration procedures to be used with their products. These procedures include unique dose calibrator settings for specific geometries (e.g., settings for measuring the activity of iodine-125 liquid in a 5 cc plastic syringe) that are based on actual tests sponsored by the manufacturers, using National Institute of Standards and Technology traceable radionuclide standards and commonly used syringes, vials, and dose calibrators.

NRC notes that some medical use licensees perform voluntary activity checks for unit dosages. When a medical use licensee finds a significant deviation between its measurement and activity on the label, the discrepancy should be resolved with the commercial nuclear pharmacy or manufacturer of the unit dosage before the licensee administers the dosage.

This IN requires no specific action nor written response. If you have any questions about the information in this notice, please contact the technical contact listed below or the appropriate NRC regional office.

**/RA/SMFrant for**

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